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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,563	07/08/2005	Eva Steiness	50412/020003	2651

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/18/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/517,563	STEINESS, EVA	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 24-39* is/are pending in the application.

4a) Of the above claim(s) *31-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22,24-30 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, remarks, and IDS submitted 3/18/10 are acknowledged.

2. Claims 31-35 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species.

Claims 1-22, 24-30, and 36-39 are under examination.

3. In view of Applicant's amendment the previous rejections under the second paragraph of 35 U.S.C. 112 have been withdrawn. In addition, the previous rejection under the first paragraph of 35 U.S.C. 112 for inadequate written description of the term "a GLP-1 related molecule having GLP-1 effect" has also been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22, 28, and 29 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of:

B) An exendin-4 analog or derivative, [now further comprising] an exendin-4, exendin-3; or an analog or derivative thereof, wherein said analog or derivative comprises an amino acid sequence at least 90% identical to exendin-4 or a fragment thereof, and said analog, derivative, or fragment increases endogenous insulin production" (Claim 22).

C) An insulin analog [now further comprising] insulin analogs that are

recognized as anti-diabetic drugs (Claim 28).

Regarding the exendin-4 analogs or derivatives, and insulin analogs of the claims, they are not described by structure or function, and few species are disclosed. Clearly, one of skill in the art would conclude that the specification fails to adequately describe these molecules. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant's arguments, filed 3/18/10, have been fully considered but are not found persuasive. Regarding B) Applicant argues that the exendin analogs of the amended claims are adequately described.

A review of the specification reveals an inadequate written description for the generic exendin analogs, and fragments thereof, of Claim 22. Note that as now recited in the claim, the fragments might be of any length, including short fragments of just a few amino acids. No such fragments with the required functional property, i.e., the ability to "increases endogenous insulin production" are disclosed. Neither are any such exendin-3's disclosed. Note that Applicant argues at page 12 of the instant Remarks that the Invention is actually the administration of a compound that functions even in it's absence, i.e., "not in continuous presence". This unexpected property has only been shown for "COMPOUND 1" and cannot be simply assumed to apply to all GLP-1 agonists, or even all exendin-4 agonists.

Regarding C) Applicant argues that the insulin analogs are "readily ascertainable by one skilled in the art" citing an FDA website search of "insulin". First note that Applicant has not indicated that date of the search. Accordingly, it is assumed that the date is recent, i.e., between the date of the last Office action (12/18/09) and the date of the filing of the instant amendment and remarks (3/18/10). A 2009/2010 search cannot demonstrate what would have been known in the art at the 2003 priority date of the instant application. Further, at the top of the newly submitted document is the warning that "Products listed on this page may not be equivalents of one another", thus, it is unclear what the products on the list actually represent. It is clear, however, this document is insufficient to establish that the specification adequately describes insulin analogs recognized as anti-diabetic drugs in 2003.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-22, 24-30, and 36-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/04156 (IDS) in view of Roach et al. (1999).

As set forth previously WO 91/04156 teaches the administration of des Pro^{36}-exendin4(1-39)-Lys_6-NH_2 (COMPOUND 1) (SEQ ID NO:5 in the instant application, SEQ ID NO:101 in the reference) for the treatment of diabetes (see particularly Claims 22 and 35 and page 16).

The reference teaching differs from the claimed invention only in that it does not teach the further administration of Lys(B28)Pro(B29) human insulin in the claimed method.

Roach et al. teach the administration of Lispro (Lys(B28)Pro(B29) human insulin) for the treatment of diabetes (see particularly the Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of treating diabetes, as taught by WO 98/58669, further comprising the administration of Lispro, as taught by Roach et al. One of ordinary skill in the art at the time of the invention would have been motivated to combine the treatments and administer both for the induction of an improved and longer-lasting response. The combining of known equivalents, in this case drugs for the treatment of diabetes, for the same purpose, in this case the lowering of blood glucose of the improved stimulation of insulin release, has long been held obvious, see *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069 (CCPA 1980). Note that the limitations of the dependent claims comprise only routine optimization and fall well within the purview of the ordinarily skilled artisan.

Applicant's arguments, filed 3/18/10, have been fully considered but are not found persuasive. Applicant argues that the primary reference, "Larsen" (WO 91/04156) fails to teach "administration of a GLP-1 agonist such that the agonist is not continuously present, as recited in claim 1 and its dependent claims".

The ordinarily skilled artisan at the time of the invention would have optimized the administration of the drug such that it would have been administered as needed. If the administration

schedule would have comprised a time such that the drug was not continuously present said schedule would have been obvious. Note that in particular for diabetics it is routine to measure blood glucose levels and administer anti-diabetic drugs as needed based on said blood glucose levels. Thus, whether or not the drug was continuously present would have been irrelevant to the diabetic; the patient would simply have taken the drug as needed.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-22, 24-30, and 36-39 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-8 of U.S. Application No. 12/277,148. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '148 application recite the treatment of diabetes with COMPOUND 1 (Claim 4) and an additional anti-diabetic human insulin analog (Claim 8) of which Lispro is an obvious well-known choice.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments, filed 3/18/10, have been fully

considered but are not found persuasive. Applicant argues that the claims of the instant application require that the GLP-1 agonist not be continuously present whereas the claims of the '148 application do not recite this requirement.

As set forth above, the claimed method would be obvious given the fact that the ordinarily skilled artisan at the time of the invention would have optimized the administration of the drug such that it would have been administered as needed. If the administration schedule would have comprised a time such that the drug was not continuously present said schedule would have been obvious. Note that in particular for diabetics it is routine to measure blood glucose levels and administer anti-diabetic drugs as needed based on blood glucose levels. Thus, whether or not the drug was continuously present would have been irrelevant to the diabetic; the patient would simply have taken the drug as needed.

10. The following are new grounds for rejection necessitated by Applicant's amendment.

11. Claims 22 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a written description rejection for the introduction of new matter into the claims.

The specification and the claims as originally filed do not provide support for the claimed method comprising:

A) The administration of an "exendin-4, exendin-3; or an analog or derivative thereof, wherein said analog or derivative comprises an amino acid sequence at least 90% identical to exendin-4 or a fragment thereof, and said analog, derivative, or fragment increases endogenous insulin production" (Claim 22).

B) The administration of at least one anti-diabetic drug wherein the "anti-diabetic drugs is insulin, an insulin analog; or a pharmaceutically acceptable mixture thereof, wherein said insulin analog is a recognized anti-diabetic drug" (Claim 28).

Regarding A), Applicant cites pages 10 and 16 in support.

A review of the cites reveals no support for 90% identical fragments of exendin-4 nor any homologs of exendin-3. Nor is there support for the functional limitation that the administered homolog "increases endogenous insulin production".

Regarding B), Applicant cites page 20 in support.

A review of the cites reveals no support for an insulin analog that is a recognized anti-diabetic drug.

12. No claim is allowed.

13. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0841.

15. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR

or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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